UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/335,686	06/18/1999	RANDOLPH J. NOELLE	012712-696	6750

909 7590 07/25/2002

PILLSBURY WINTHROP, LLP
P.O. BOX 10500
MCLEAN, VA 22102

EXAMINER	
GAMBEL, PHILLIP	
ART UNIT	**PAPER NUMBER**
1644	18

DATE MAILED: 07/25/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/335686	NOELLE
	Examiner	Art Unit
	GAMBEL	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☑ Responsive to communication(s) filed on 3/18/02; 5/16/02

2a)☐ This action is **FINAL**. 2b)☑ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☑ Claim(s) _____ is/are pending in the application. 44-46, 49-55

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☑ Claim(s) _____ is/are rejected. 44-46, 49-55

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☑ The translation of the foreign language provisional application has been received.

15)☑ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114.

Applicant's submission (Paper No. 17), filed on 5/16/02, has been entered.

Applicant's amendment, filed 3/18/02 (Paper No. 14), has been entered.
Claim 44 has been amended.

Claims 44-46 and 49-55 are pending and being acted upon presently

Claims 1-43 and 47/48 have been canceled previously.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Office Action will be in response to applicant's arguments, filed 3/18/02 (Paper No. 14).
The rejections of record can be found in the previous Office Actions (Paper Nos. 9/11/15).

3. Claims 44-46 and 49-55 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. The specification as originally filed does not provide support for the invention as now claimed: "wherein prolonged humoral immune means that suppression of antibody prevention against the TD antigen is maintained after administration of said anti-gp39 has been terminated".

Applicant's amendment, filed 3/18/02 (Paper No. 14), directs support for the instant claimed limitations to page 13, lines 5-10 of the instant specification.

Applicant asserts that the present invention clearly envisioned the invention as-filed.
Previously, applicant argued that the originally specification provides ample support for a similar claimed limitation, by pointing to page 12 which defines prolonged suppression to mean that suppression of the antibody production against a TD antigen is maintained after administration of a gp39 antagonist in vivo has been terminated. Applicant also pointed to pages 20, 21 and 25 and Figures 1B and 6B which address the half-life of anti-gp39 antibodies.

In contrast to applicant's assertions, the disclosure of the limitation "wherein prolonged humoral immune means that suppression of antibody prevention against the TD antigen is maintained after administration of said anti-gp39 has been terminated" is not readily apparent in the specification as filed. The specification as filed does not provide sufficient written description for this "limitation". The specification does not provide blazemarks nor direction for the instant methods encompassing the above-mentioned "limitation", as currently recited. Neither the scope nor the metes and bounds of the maintenance of antibody suppression is clearly disclosed in the application as filed. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office action

Alternatively, applicant is invited to provide sufficient written support for the "limitations" indicated above. See MPEP 714.02 and 2163.06

Applicant's arguments are not found persuasive.

4. Claims 44-46, 49 and 51-53 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Cobbold et al. (U.S. Patent No. 6,056,956) in view of Lederman et al. (U.S. Patent No. 5,474,771; 1449, #AA) OR Armitage et al. (U.S. Patent No. 6,087,329) for the reasons of record set forth in Paper Nos. 9/11/15.

Claims 50, 54, 55 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Cobbold et al. (U.S. Patent No. 6,056,956) in view of Lederman et al. (U.S. Patent No. 5,474,771; 1449, #AA) OR Armitage et al. (U.S. Patent No. 6,087,329).
as applied to claims 44- 46, 9, 51-53 above
and in further view of Ramanathan et al. (WO 91/09059) for the reasons of record set forth in Paper No. 9/11/15.

5. Applicant's arguments, filed 3/18/02 (Paper No. 14), have been fully considered but are not found convincing essentially for the reasons of record.

Applicant's arguments and the examiner's rebuttal are essentially the same as of record.

Applicant maintains that none of the references teach or suggest concurrent administration of a soluble TD antigen (e.g. a therapeutic antibody) and a gp39 antagonist to achieve prolonged suppression of the humoral immunity wherein prolonged suppression of immunity means that antibodies against TD antigen remain suppressed after gp39 antibody administration has been terminated.

While applicant acknowledge that Cobbold teach the use of CD4 antibodies to induce tolerance to an antigen, applicant argues that Cobbold does not suggest that an anti-gp39 antibody can be used to tolerize a host against a specific antigen. Applicant argues that it would have been unpredictable to achieve tolerance or long term suppression with an antibody to another T cell antigen.

While applicant acknowledges that Lederman et al. and Armitage et al. teach the use of anti-gp39 antibodies to suppress humoral immunity in a global manner to a plurality of antigens, these references do not teach nor suggest the co-administration of an anti-gp39 antibody and a soluble TD antigen to achieve prolonged tolerance to a specific TD antigen, including after gp39 antibody administration has been discontinued.

Applicant argues that the instant invention surprisingly discovered that a gp39 antibody had prolonged effect on T cell function and specifically resulted in the inability of T cells to respond to specific antigens to which they become exposed in conjunction with a gp39-specific antibody and that this prolonged suppression was not suggested by the prior art of Cobbold, Lederman and Armitage. Applicant asserts that these prior art references teach only that a gp39-specific antibody would have a transient, global effect on antibody production by B cells and are silent on the prolonged effect on a gp39 antagonist on T cells.

Applicant asserts that Ramanthan et al. Is silent with respect to anti-gp39 antagonists on allergic responses and on the prolonged antigen specific on T cells.

In contrast to applicant assertions, the following of record is set forth to support the motivation and expectation of success at the time the invention was made to achieve the claimed limitations.

Cobbold et al. teach the use of CD4-specific antibodies to induce specific non-responsiveness or tolerance to various molecules, including globular proteins, glycoproteins and polypeptides intended for therapeutic use and allergens (see entire document; including column 2, paragraph 4; column 3, paragraphs 5-6).

Cobbold et al. teach the combined preparation for simultaneous, separate or sequential administration of antibody treatment to induce tolerance to an antigen (see column 2, paragraph 3), including a number of antigens (see column 2, paragraph 4). Cobbold et al. further teach that the antigen can be given at the time the course the immunosuppressive antibody treatment is commenced, that is, tolerance to an antigen can be induced under the cover to administering immunosuppressive antibodies (see column 3, paragraphs 5-6).

Cobbold et al. differ from the claimed methods by not teaching the preferred embodiments of targeting the CD40L/gp39 expressed on T cells with CD40L-specific antibodies.

Lederman et al. teach inhibiting various immune responses with 5C8-specific antibodies (see entire document, including columns 6-7, 11); including allergies (column 11, paragraph 6). The 5C8 specificity is the equivalent of human CD40L. Ldederman et al. Teach effective inhibiting amounts, including amounts to inhibit T cell activation of B cells (see columns 10-11, overlapping paragraph). In addition, Lederman et al. also teach inhibiting immune responses such as transplant rejection and autoimmunity, responses associated with T cells (see column 11, paragraphs 4-5).

Armitage et al. teach inhibiting various immune responses with CD40 antagonists, including soluble CD40, CD40Ig, monomeric CD40L (e.g. columns 10-11, including overlapping paragraph, columns 14-17; column 21); including targeting allergies, including IL-4 induced IgE responses (e.g. column 10, paragraph 3 - column 11, paragraph 1; column 15, paragraph 1-2; Examples 8-11, 13).

In contrast to applicant's assertions of no connection between targeting CD4 and CD40L/gp39; the prior art of Cobbold et al., Lederman et al. and Armitage et al. all target the same cell, that is, the CD4 T helper cell with the motivation and expectation of success of inhibiting immune response to a broad variety of antigens, given the essential role of T helper cells in immune responses and regulation.

Also, in contrast to applicant's assertions, the prior art does teach achieving specific non-responsiveness or specific unresponsiveness to antigens of interest, including those thymus-dependent antigens encompassed by the claimed methods.

Given such specific unresponsiveness, the long term specific unresponsiveness would have been expected to be maintained for a prolonged period of time, including after clearance of CD40L-specific antibodies. This is not to say that additional treatment could be forthcoming but the ordinary artisan would have expected that prolonged suppression would have been achieved by achieving the endpoint of specific nonresponsiveness at the time the invention was made.

Given the ability of 5C8-/CD40L-specific antibodies, as taught by Lederman et al. OR the ability of various CD40 antagonists, as taught by Armitage et al. to inhibit various immune responses, including T helper cell-mediated immune responses, including humoral responses; one of ordinary skill in the art at the time the invention was made would have been motivated to substitute these antagonists into the methods of Cobbold et al. to similarly target T helper cells to inhibit humoral responses to thymus-dependent antigens. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Also, as pointed out previously, the following is noted.

Ramanathan et al. teach the use of IL-4-specific antagonists such as IL-4-specific antibodies to inhibit or treat allergic responses (see entire document, including page 1, paragraph 3; Summary of the Invention; Description f the Invention, page 6, paragraph 2, pages 13-16).

Combination therapy was known and practiced at the time the invention was made.

It was prima facie obvious to combine two compositions each of which is taught by prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose; idea of combining them flows logically from their having been individually taught in prior art. In re Kerkhoven, 205 USPQ 1069, CCPA 1980. See MPEP 2144.

Given the prior art teachings of using both CD40:CD40L-specific inhibitors and IL-4-specific inhibitors to inhibit allergic responses; the ordinary artisan would have been motivated to combine both said inhibitors to down regulate responses to allergens at the time the invention was made.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments are not found persuasive.

6. Claims 44-46 and 49-55 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-17 of U.S. Patent No. 5,942,229 for the reasons of record set forth in Paper No. 9.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the patented claims anticipate the instant method claims.

In addition, when the instant claims are read in light of the specification; the patented claims are the preferred embodiments and again anticipate the instant claims.

Applicant's amendment, filed 9/24/01 (Paper No. 10), requests that this rejection be stayed in abeyance until the subject application is otherwise in condition for allowance.

7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Phillip Gambel, Ph.D.
Primary Examiner
Technology Center 1600
July 24, 2002

John J. Doll, Director
Technology Center 1600